THE RELATION BETWEEN FUNCTIONAL TESTS AND THE PATHOLOGICAL ANATOMY OF THE KIDNEY IN CHRONIC NEPHRITIS.

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Is it possible to tell during life what type of chronic nephritis from the pathologists' view-point is present in the individual case?

Before taking up that question it is important to define what is meant by chronic nephritis and what classification from the pathologists' view-point is the most satisfactory.

It seems most reasonable to consider as chronic nephritis any progressive destruction of the kidney parenchyma resulting from either some infectious agent or some bacterial, metabolic, or chemical poison. The process may start insidiously or follow some outspoken acute disturbance in the kidney. In some cases more than one cause may be present. In other cases a primary injury to the kidney by bacteria or other toxins may upon healing leave too little kidney substance to carry on renal function, so that gradually the remaining kidney tissue goes to pieces under the strain of its routine work. It must also be remembered that acute injury to the renal parenchyma may heal with scar formation and still have the remaining portions of the kidney function normally without any progressive degenerative changes starting in the kidney. Examples of such a condition vary from the isolated sclerosed glomeruli occasionally observed in children's kidneys up to the extensive scarring seen following acute bacterial infections which have healed. Such cases should be looked upon by both pathologist and clinician as healed nephritis and not chronic nephritis.

Although it is evident from the above that chronic nephritis covers a large field of renal conditions, this study will be simplified by leaving out of consideration those cases of chronic nephritis due to the presence of infective agents in the kidney. Certain of the cases reported may have been examples of a chronic nephritis starting upon the scarred kidney resulting from the healing of such an infection.

This work, therefore, narrows itself down to a consideration of those types of chronic nephritis which are usually met with in the medical wards of a hospital that come to a fatal termination. It must be remembered that the amount of kidney destruction in chronic nephritis varies considerably with the duration of the process, and that we rarely have a chance to study at autopsy the cases in the early stages of the progressive kidney disease.

In turning to a pathological classification for chronic nephritis one naturally meets most frequently the old terms chronic parenchymatous nephritis and chronic interstitial nephritis. The application of these terms to clinical conditions and in pathological studies has been rather loose. Furthermore, they do not suggest in the name what is the fundamental lesion in the kidney.

In Mallory's[1] recent book, the classification of nephritis for this group of cases is taken up from the view-point of what part of the kidney tissue is primarily involved. From the name, therefore, one may learn the original focus of the renal involvement, and from that realize just what has been going on in the kidney from the time of the original injury down to the end result.

Mallory, in this classification, speaks of tubular nephritis, capsular-glomerulonephritis, intracapillary-glomerulonephritis, and vascular nephritis. The lesions in any kidney may be of one type or a combination of several types. He mentions a variety of acute lesions which may occur in the first three of these types in that part of the kidney specified in the name. Some of these acute lesions heal without producing a permanent injury in the kidney. Many of them, however, on healing produce a permanent scar in the kidney with subsequent progressive degeneration of the renal parenchyma.

The types of acute nephritis which on healing are apt to turn into a chronic progressive nephritis are certain forms of the acute capsular-glomerulo and the acute intracapillary-glomerulo. It is the early stages of these types of progressive kidney destruction which are commonly considered clinically as chronic parenchymatous nephritis.

The chronic vascular nephritis usually results from simple arteriosclerosis of the smaller renal arteries, but may follow some acute lesion of the smaller renal vessels which upon healing causes impaired circulation with resulting progressive lesions in the vessels and renal parenchyma.

In the chronic vascular type secondary changes take place in the glomeruli supplied by the involved vessels, with eventual sclerosis of all or a part of the tuft. In the two glomerulo types usually the greater number of the glomeruli are involved, with eventual sclerosis of part or all of the capsules or tufts of both. In all three of the types following the injury to the glomeruli, secondary degenerative changes occur in the tubules. These may consist of atrophy and disappearance of the tubules or dilatation with atrophy of the lining epithelium.

Mallory is uncertain whether any actual proliferation takes place in the connective tissue of the kidney, but feels there is certainly a relative increase as the parenchyma disappears. The connective tissue is frequently invaded with cells of the lymphocytic series.

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[1] Principles of Pathological Histology, 1914.

In this study the classification of nephritis suggested by Mallory has been followed, as it seems to be much more comprehensive than the older classifications. It was surprising how readily one could put the kidney into the proper group from examination of a single section under the microscope. Dr. Mallory has been kind enough to go over the slides and confirm the group into which each kidney belongs.

Up to the present time eighteen cases of chronic nephritis have come to autopsy at the Peter Bent Brigham Hospital, upon which enough clinical work has been done to make them of interest for comparison between the clinical and anatomical findings.

Unfortunately, as most of the cases were naturally seriously ill, it was not possible to put them on standard diets and learn their ability to put out added salt and urea which have been found at this hospital[2] to be of value in diagnosis and prognosis respectively of chronic nephritis. In most of the cases, however, the following four tests for diagnosis and prognosis of chronic nephritis were carried out: Examination of urine for albumin or casts, blood-pressure determinations, phenolsulphonephthalein excretion test, and estimation of non-protein nitrogen in the blood. In addition to reporting the results of these tests, record has been made of the age of the patient, the presence or absence of edema at the time of entrance, the examination of the eye-grounds, the previous acute infections, the result of the Wassermann serum reaction, and any complicating conditions at the time of death. This data was obtained from the medical records of the hospital.

It also seemed of interest to note the gross pathological findings at autopsy in order to see if it were possible to place these cases in their proper groups without the aid of the microscope. For this purpose the weight of the two kidneys, the width of the cortex, the adherence of the capsule, and the appearance of the surface of the kidney under the capsule were noted. This data was obtained from the pathological records of the hospital.

All this data is presented in the form of two tables, one containing the cases of chronic vascular nephritis, the other the cases of chronic glomerulonephritis. Most of the glomerulo cases were a combination of capsular-glomerulo and intracapillary-glomerulo. It is evident the majority of the cases are of the chronic vascular type.

Of the 14 cases considered as chronic vascular nephritis 1 was possibly a congenital malformation of the kidney and 2 were possibly healed acute infections which had involved other parts of the kidney besides the vessels and in which progressive renal destruction was going on. The weight of the kidneys varied from 360 grams to 42 grams. The capsule was adherent in 6 and stripped easily in 8. The surface of the kidney was granular or rough in 12 and smooth in 2. The cortex varied from 8 mm. to 1 mm. In the 4 cases of chronic glomerulonephritis one showed the process in its early stages probably not more than a few weeks or months. The weights varied from 435 grams to 155 grams. In 3 the capsule stripped easily, in 1 there was a slight resistance. The cortex varied from 14 mm. to 4 mm. The surface was smooth in 3 and granular in 1. It is thus evident that the kidneys can not be put with certainty into the proper group from the gross appearance alone. However, in the glomerulo type the capsule usually strips readily, leaving a smooth surface, while in the vascular type the surface is usually granular and the capsule more apt to be adherent.

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[2] Frothingham, The Value of Certain Tests for Diagnosis and Prognosis in Chronic Nephritis, Amer. Jour. Med. Sci., June, 1915.

All but 2 of the cases of chronic vascular nephritis showed albumin on the first or second examination of the urine, and these 2 occasionally did; 3 showed no casts on repeated examinations; 3 showed them only rarely, and the others showed casts pretty constantly. The blood-pressure on entrance in all cases but two was above 150 mm. of mercury. The pulse pressures varied from 100 to 40 mm.

In none of the 13 cases in which the 'phthalein test was done was the elimination for two hours above 40, and several showed no excretion in that time. The non-protein nitrogen of the blood was estimated in 11 of the cases, and in all but one was elevated above 30 mgm. per 100 c.c., which is considered normal when estimated by the Folin and Denis method. In some cases it went as high as 250+ mgm. per 100 c.c. of blood. These very high estimations were found in the blood usually just a short time before death, and probably represent a sudden terminal rise in non-protein nitrogen, which has frequently been noted in the last days of life in cases which have shown pronounced uremic symptoms for some time. Edema was present in 8 cases and absent in 6. In 6 of the 8 cases with edema, myocarditis was recorded as a complicating factor. In 5 of the 11 cases of chronic vascular nephritis in which eyegrounds were examined, no lesions were noted. In the other 6 there was edema, hemorrhages, or exudate, and in some all three. In 2 cases the Wassermann serum reaction was positive. In this group the ages varied from twenty-four to seventy-one years.

In the group of chronic glomerulonephritis albumin and casts were present in all cases. The blood-pressure was elevated above 150 mm. of mercury in 2 and not in the others. The pulse pressure varied from 80 to 45 mm. The phenolsulphonephthalein output was diminished in all 4 cases ranging from 22 in one and a half hours to 0 in two hours. In only 2 cases was the non-protein nitrogen of the blood estimated, and in those 2 it was above 100 mgm. per 100 c.c. Edema was present in 2 cases and absent in 2. In the 2 cases with edema there was no evidence of chronic cardiac

CHRONIC VASCULAR NEPHRITIS.

Hospital Med. No.	Kidney.				Age.	Urine.		Blood-pressure.		Pulse pressure.	Per cent. phthalein in 2 hrs.	Mgms. nitrogen per 100 c.c.	Edema.	Eye grounds.	Wassermann reaction.	Past acute infections.	Complications.
	Surface.	Wht. of both.	Cortex	Capsule.		Albumin.	Casts	Systolic.	Diastolic.								
		Gm.	mm.														
328	Very rough	330	8.0	Adherent	61	+	+	170	110	60	31.0	–	+	No edema. No hemorrhage; no exudate	Not done.	Measles, pertussis, smallpox and acute rheumatism	Myocarditis.
673	Rough	195	4.0	Adherent	32	+	Rare	180	125	55	0	200	0	Not done	++	Measles, osteomyelitis with 7 operations	Fibrous pericarditis.
655	Rough	190	2.0	Strips easily	30	+	+	230	140	90	28.0	90	0	Hemorrhages; exudate; no edema	Negative	Dobie itch, dysentery, frequent tonsillitis, gonorrhea, malaria	None.
895	Granular	90	2.0	Strips easily	50	Rare	0	205	130	75	0	100	+	No edema; no hemorrhage; no exudate	Negative	Measles, chicken-pox, pertussis, bilious attacks	None.
1124	Finely granular	230	–	Strips easily	63	+	+	130	80	50	31.0	62	+	No edema; no hemorrhage; no exudate	Negative	Measles, mumps, pertussis, scarlet fever, acute rheumatism	Myocarditis; aortic insufficiency.
4	Rough	160	5.0	Slightly adherent	63	+	+	240	140	100	12.0	–	0	Exudate; no hemorrhage; no edema	Negative	None recorded	None.
1640	Granular	42	3.0	Adherent	24	+	0	120	68	52	0	204	0	No exudate; no hemorrhage; no edema	Negative	Measles, pertussis, chicken-pox, scarlet fever, sore throats	Possibly congenital malformation of kidney.
1593	Rough	90	1.0	Strips easily	31	+	+	238	138	100	3.0	56 to 138	0	Edema; exudate; hemorrhage	Negative	Measles, pertussis, chicken-pox, scarlet fever, typhoid. Convulsions at age (8–10)	None.
1975	Smooth	360	5.0	Strips easily	39	+	+	208	152	56	–	257.7	+	Edema; exudate; hemorrhage	Negative	Measles, erysipelas, typhoid	None.
1844	Rough	280	4.0	Slightly adherent	71	Rare	Rare	155	95	60	17.0	25	+	Not done	Negative	Measles, malaria	Myocarditis, auricular fibrillation, hemiplegia.
1405	Granular	310	3.5	Slightly adherent	59	+	Rare	175	130	45	40.5	–	+	Not done	Negative	Measles, acute rheumatism, gonorrhea, chancre	Myocarditis, auricular fibrillation, arteriosclerosis.

2008	Smooth	330	1.5	Strips easily	45	+	+	190	98	92	0	80	0	No edema; no exudate; no hemorrhages	+	Diphtheria, pneumonia scarlet fever, measles, whooping cough, mumps, typhoid	Marked amyloid in kidney glomeruli, myocarditis, mitral *regurgitation.*
2111	Granular	220	2.5	Strips easily	52	+	0	180	120	60	10.0	Urea 55.5	+	Slight edema; no hemorrhages; no exudate	Negative	Mumps, measles, pertussis, typhoid-pneumonia, broken arm	Myocarditis, arteriosclerosis, pericarditis.
2108	Granular	284	Markings vague	Strips easily	28	+	+	100	150	40	22.0	47.5	+	Edema; exudate; slight hemorrhage	Negative	Croup as a baby, moderate drinker up to 5 years ago. Dull red urine twice 6 yrs. ago.	Myocarditis, possibly old, healed intracapillary glomerulo lesion.

CHRONIC GLOMERULONEPHRITIS.

81	Smooth	435	11.0	Strips easily	26	+	+	140	85	55	22 in. 1¼ hrs.	–	+	Not done	Not done	Chorea, some septic or tubercular chest condition, grippe	Pneumonia. Subacute nephritis of the intracapillary type.
254	Smooth	314	8.0	Strips easily	38	+	+	100	115	45	4.0	–	+	Slight edema; no hemorrhage; no exudate	Negative	Scarlet fever, typhus, rheumatic fever, ovary operation	Pericarditis, pleurisy, cystitis. Both intracapillary and capsular types.
1283	Granular	155	4.0	Slightly adherent	16	+	+	140	85	55	0	117	0	No exudate; no hemorrhage; no edema.	Negative	Measles, mumps, diphtheria, scarlet fever, chicken-pox, sore throats, *pertussis*	None. Both intracapillary and capsular types.
1860	Smooth	310	9.0	Strips easily	19	+	+	105	115	80	Trace	112	0	No edema; no hemorrhage; no exudate	Negative	Scarlet fever, measles, otitis media, frequent sore throats	None. Intracapillary type.

disease. In 3 of the cases of chronic glomerulonephritis the eye-grounds were studied, and except for slight edema in one no abnormal findings were noted. The Wassermann serum reaction was negative in the 3 cases in which it was done. The ages of these 4 cases ranged from thirty-eight to sixteen years, which is lower than those of the other group. There were, however, many cases of the vascular type within these age limits.

From a study of this small group of cases of chronic glomerulonephritis it is evident that it will not be possible by means of the four tests for renal disease mentioned above to tell definitely into which group a given case of nephritis belongs. The age of the patient, the presence or absence of edema or pulse pressure also does not give any assistance in this direction. Changes in the eye-grounds were not constant enough in either group to aid in classifying the cases. The previous history is not of assistance, for although most of the cases of glomorulonephritis had scarlet fever, still many of the cases of chronic vascular nephritis that died young also had had scarlet fever. It must be remembered that these cases are all ones of pronounced nephritis in the end stages. It is possible that by the more complicated dietary tests for renal function which may be carried out on the patients not so ill a grouping of the cases according to the pathological lesions may be accomplished. Possibly, therefore, at some future date enough of the chronic nephritis cases that have been studied in this hospital by these more elaborate methods will come to autopsy here to settle this question.

Grouping all these cases for clinical purposes simply as chronic nephritis of a severe grade, it is interesting to note that the non-protein nitrogen of the blood was elevated in all cases but one in which it was examined, and that one may well have died of cardiac and cerebral complications. The ability of the kidney to excrete phenolsulphonephthalein was diminished in all the cases in which it was done. Albumin was present in the first or second urine examinations in all cases but 2. Casts were not found in 3 cases and only rarely in 3 more. The blood-pressure was above 150 in all but 4 of the cases; 7 of the 14 cases in which the fundi were examined showed lesions in the eye-grounds.